

General

Guideline Title

Practice parameter: evaluation of the child with microcephaly (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society.

Bibliographic Source(s)

Ashwal S, Michelson D, Plawner L, Dobyns WB, Quality Standards Subcommittee of the American Academy of Neurology, Practice Committee of the Child Neurology Society. Practice parameter: Evaluation of the child with microcephaly (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. *Neurology*. 2009 Sep 15;73(11):887-97. [40 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

The American Academy of Neurology reaffirmed the currency of this guideline in 2013.

Recommendations

Major Recommendations

Definitions of the levels of the recommendations (A, B, C, U) and classification of the evidence (Class I-IV) are provided at the end of the "Major Recommendations" field.

What is the role of diagnostic testing of children with microcephaly?

Neuroimaging

Conclusions

Data from 6 Class III studies (2 computed tomography [CT], 2 magnetic resonance imaging [MRI], 2 CT/MRI) of 292 children with microcephaly found diagnostic yields ranging from 43% to 80%. In 2 studies, children with severe microcephaly (<-3 SD) were more likely (i.e., 75%, 80%) to have an abnormal MRI than those with milder microcephaly. MRI detected brain abnormalities typically beyond the sensitivity of computed tomography (CT).

Recommendation

Neuroimaging may be considered useful in identifying structural causes in the evaluation of the child with microcephaly (Level C).

Genetic Testing

Conclusions

Genetic etiologies may be found in 15.5% (Class II, n = 58) to 53.3% (Class III, n = 30) of children with microcephaly. MRI studies may detect specific malformations associated with well described genetic conditions.

Recommendation

Specific targeted genetic testing may be considered in the evaluation of the child with microcephaly in order to determine a specific etiology (Level C).

Metabolic Testing

Conclusions

The prevalence of metabolic disorders among children with microcephaly is unknown. Based on prior analysis of studies of children with global developmental delay (GDD), it is likely 1% to 5%.

Recommendation

There is insufficient evidence to support or refute obtaining metabolic testing on a routine basis for the evaluation of the newborn or infant with microcephaly (Level U).

What neurologic disorders are associated with microcephaly?

Epilepsy

Conclusions

Children with microcephaly are more likely to have epilepsy, particularly epilepsy that is difficult to treat. Certain microcephaly syndromes are associated with a much higher prevalence of epilepsy. There are no systematic studies regarding electroencephalogram (EEG) testing of children with microcephaly with and without epilepsy.

Recommendations

1. Because children with microcephaly are at risk for epilepsy, physicians may consider educating caregivers of children with microcephaly on how to recognize clinical seizures (Level C).
2. There are insufficient data to support or refute obtaining a routine EEG in a child with microcephaly (Level U).

Cerebral Palsy (CP)

Conclusions

CP is a common disability in children with microcephaly. Microcephaly, particularly of postnatal onset and identifiable etiology, is more common in children with CP.

Recommendations

1. Because children with microcephaly are at risk for CP, physicians and other care providers may consider monitoring them for early signs so that supportive treatments can be initiated (Level C).
2. Because children with CP are at risk for developing acquired microcephaly, serial HC measurements should be followed (Level A).

Mental Retardation

Conclusions

Microcephaly is commonly found in developmentally and cognitively impaired children. Children with microcephaly are at a higher risk for mental retardation and there is a correlation between the degree of microcephaly and the severity of cognitive impairment.

Recommendation

Because children with microcephaly are at risk for developmental disability, physicians should periodically assess development and academic achievement to determine whether further testing and rehabilitative efforts are warranted (Level A).

Ophthalmologic and Audiologic Disorders

Conclusions

Ophthalmologic disorders are more common in children with microcephaly but the frequency, nature, and severity of this involvement has not been studied. Data on the prevalence of audiologic disorders in children with microcephaly have not been reported.

Recommendations

Screening for ophthalmologic abnormalities in children with microcephaly may be considered (Level C).

Definitions:

Classification of Recommendations

Level A = Established as effective, ineffective, or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.*)

Level B = Probably effective, ineffective, or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

Level C = Possibly effective, ineffective, or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

Level U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if: 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

Classification of Evidence for the Rating of a Screening Article

Class I: A statistical, population-based sample of patients studied at a uniform point in time (usually early) during the course of the condition. All patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation that is masked to the patients' clinical presentations.

Class II: A statistical, non-referral-clinic-based sample of patients studied at a uniform point in time (usually early) during the course of the condition. Most patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation that is masked to the patients' clinical presentations.

Class III: A sample of patients studied during the course of the condition. Some patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation by someone other than the treating physician.

Class IV: Studies not meeting Class I, II or III criteria including consensus, expert opinion or a case report.

Clinical Algorithm(s)

The original guideline document contains clinical algorithms for:

- Evaluation of congenital microcephaly
- Evaluation of postnatal onset microcephaly

Scope

Disease/Condition(s)

Microcephaly

Guideline Category

Counseling

Diagnosis

Evaluation

Risk Assessment

Screening

Clinical Specialty

Family Practice

Medical Genetics

Neurology

Nuclear Medicine

Pediatrics

Physical Medicine and Rehabilitation

Radiology

Intended Users

Advanced Practice Nurses

Nurses

Physical Therapists

Physician Assistants

Physicians

Guideline Objective(s)

To make evidence-based recommendations concerning the evaluation of the child with microcephaly

Target Population

Children with head circumferences more than 2 standard deviations below the mean for age and gender

Interventions and Practices Considered

1. Neuroimaging
2. Targeted and specific genetic testing
3. Metabolic testing
4. Screening for coexistent conditions such as cerebral palsy, epilepsy, and sensory deficits

Major Outcomes Considered

- Diagnostic yield

- IQ
- Academic achievement scores
- Head growth pattern
- Associated developmental problems

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

2009 Guideline

Literature searches were conducted with the assistance of the University of Minnesota Health Science Center for relevant articles published from 1980 to March 2007. Medline, CINAHL, and Healthstar databases were searched for relevant articles published from 1966 to 2007, using the following key words: microcephaly, magnetic resonance imaging, MRI, computed axial tomography, CT scan, metabolic disease, electroencephalography (EEG), seizures, epilepsy, vision loss, hearing loss, developmental delay, and speech and language delay. The search resulted in 4,257 titles and abstracts, which were reviewed for content regarding the diagnostic evaluation of children with microcephaly. Articles were excluded if they were Class IV studies, case series with less than 10 subjects, descriptions of research in animals, or descriptions of a single cause of syndromic microcephaly. The authors selected 150 articles for review. The ages of infants and children included in these studies were similar to the ages of children typically seen for diagnostic evaluation so it was felt that the evidence-based recommendations included in this parameter were appropriate.

2013 Reaffirmation

The guideline developer searched OVID MEDLINE, CINAHLScience, and Healthstar for studies published between 2010 and 2013 using the following search terms: microcephaly, magnetic resonance imaging, MRI, computed axial tomography, CT scan, metabolic disease, electroencephalography (EEG), seizures, epilepsy, vision loss, hearing loss, developmental delay, and speech and language delay.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Classification of Evidence for the Rating of a Screening Article

Class I: A statistical, population-based sample of patients studied at a uniform point in time (usually early) during the course of the condition. All patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation that is masked to the patients' clinical presentations.

Class II: A statistical, non-referral-clinic-based sample of patients studied at a uniform point in time (usually early) during the course of the condition. Most patients undergo the intervention of interest. The outcome, if not objective, is determined in an evaluation that is masked to the patients' clinical presentations.

Class III: A sample of patients studied during the course of the condition. Some patients undergo the intervention of interest. The outcome, if not

objective, is determined in an evaluation by someone other than the treating physician.

Class IV: Studies not meeting Class I, II or III criteria including consensus, expert opinion or a case report.

Methods Used to Analyze the Evidence

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Each article was reviewed and classified by two committee members. Data reviewed included first author, year, study population, study design, number of patients, types of microcephaly, results of testing, and outcomes measured. A four-tiered classification scheme for determining the yield of established diagnostic and screening tests developed by the Quality Standards Subcommittee was utilized as part of this assessment (see the "Rating Scheme for the Strength of the Evidence" field).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

2009 Guideline

Depending on the strength of this evidence, it was decided whether specific recommendations could be made, and if so, the level of strength of these recommendations (see the "Rating Scheme for the Strength of the Recommendations" field).

2013 Reaffirmation

The AAN assesses their clinical practice guidelines every 2 years to determine whether new literature has been published that would warrant an update. The following steps are taken:

- Biennial correspondence is sent to all authors and the facilitator.
- An updated literature search and a review of methodological soundness are performed by a Guideline Development Subcommittee (GDS) member. (Note: The search should specifically seek to identify new evidence that would change the conclusions in the systematic review or recommendations in the CPG.)

All documents biennially reviewed by the GDS that don't require an update are reaffirmed. See the AAN [Clinical Practice Guideline Process Manual](#) for additional information.

Rating Scheme for the Strength of the Recommendations

Classification of Recommendations

Level A = Established as effective, ineffective, or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.*)

Level B = Probably effective, ineffective, or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)

Level C = Possibly effective, ineffective, or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)

Level U = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if: 1) all criteria are met, 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The guideline was approved by the Quality Standards Subcommittee on November 5, 2008; by the Child Neurology Society (CNS) Practice Committee on August 2, 2009; by the American Academy of Neurology (AAN) Practice Committee on November 20, 2008; and by the AAN Board of Directors on July 7, 2009.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

More accurate classification of the microcephalic child

Potential Harms

Not stated

Qualifying Statements

Qualifying Statements

This statement is provided as an educational service of the American Academy of Neurology (AAN). It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved. The clinical context section is made available in order to place the evidence-based guideline(s) into perspective with current practice habits and challenges. No formal practice recommendations should be inferred.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

Foreign Language Translations

Patient Resources

Quick Reference Guides/Physician Guides

Resources

Staff Training/Competency Material

Wall Poster

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

IOM Domain

Effectiveness

Identifying Information and Availability

Bibliographic Source(s)

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2009 Sep 15 (reaffirmed 2013 Nov)

Guideline Developer(s)

American Academy of Neurology - Medical Specialty Society

Child Neurology Society - Medical Specialty Society

Source(s) of Funding

American Academy of Neurology (AAN)

Guideline Committee

American Academy of Neurology Quality Standards Subcommittee

Child Neurology Society Practice Committee

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Disclosure

Dr. Ashwal serves on the scientific advisory board of the Tuberous Sclerosis Association and the International Pediatric Stroke Society; serves as an editor of *Pediatric Neurology*; and receives research support from the NIH [1 R01 NS059770-01A2 (PI), 1 R01 NS054001-01A1 (PI), and R01 CA107164-03 (PI)]. Dr. Michelson reports no disclosures. Dr. Plawner receives royalties from publishing PEMSoft: The Pediatric Emergency Medicine Software (2007 and 2008); receives research support from the NIH [NO1-HD-3-3351 (Co-investigator)]; and has served as an expert consultant in a legal proceeding. Dr. Dobyns serves on the editorial advisory boards of the *American Journal of Medical Genetics* and *Clinical Dysmorphology* and receives research support from the NIH [1R01-NS050375 (PI) and 1R01-NS058721 (PI)].

Conflict of Interest Statement

The American Academy of Neurology (AAN) is committed to producing independent, critical, and truthful clinical practice guidelines (CPGs). Significant efforts are made to minimize the potential for conflicts of interests to influence the recommendation of this CPG. To the extent possible, the AAN keeps separate those who have a financial stake in the success or failure of the products appraised in the CPGs and the developers of the guidelines. Conflict of interest forms were obtained from all authors and reviewed by an oversight committee prior to project initiation. AAN limits the participation of authors with substantial conflicts of interest. The AAN forbids commercial participation in, or funding of, guideline projects. Drafts of the guidelines have been reviewed by at least three AAN committees, a network of neurologists, *Neurology*® peer reviewers, and representatives from related fields. The AAN Guideline Author Conflict of Interest Policy can be viewed at www.aan.com

Guideline Status

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The American Academy of Neurology reaffirmed the currency of this guideline in 2013.

Guideline Availability

Electronic copies: A list of American Academy of Neurology (AAN) guidelines, along with a link to a Portable Document Format (PDF) file for this guideline, is available at the [AAN Web site](#) .

Print copies: Available from the AAN Member Services Center, (800) 879-1960, or from AAN, 201 Chicago Avenue South, Minneapolis, MN 55415.

Availability of Companion Documents

The following are available:

- Practice parameter: evaluation of the child with microcephaly (an evidence-based review). American Academy of Neurology (AAN) guideline summary for clinicians. St. Paul (MN): American Academy of Neurology. 2009 Sep. 2 p. Available in Portable Document Format (PDF) from the [American Academy of Neurology \(AAN\) Web site](#) .
- Practice parameter: evaluation of the child with microcephaly (an evidence-based review). Case study. St. Paul (MN): American Academy of Neurology. 2009. 3 p. Available in PDF from the [AAN Web site](#) .
- Practice parameter: evaluation of the child with microcephaly (an evidence-based review). Poster. St. Paul (MN): American Academy of Neurology. 2009. 1 p. Available in PDF from the [AAN Web site](#) .
- AAN guideline development process [online]. St. Paul (MN): American Academy of Neurology. Available from the [AAN Web site](#) .

In addition, a Turkish translation is available from the [Neurology Journal Web site](#) .

Patient Resources

The following is available:

- Evaluation of the child with microcephaly. American Academy of Neurology (AAN) summary of evidence-based guideline for patients and their families. 2009. 2 p. Available in Portable Document Format (PDF) is available from the [AAN Web site](#) .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

This NGC summary was completed by ECRI Institute on September 1, 2010. The currency of the guideline was reaffirmed by the developer in 2013 and this summary was updated by ECRI Institute on May 27, 2015.

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